CLAIMS

What is claimed is:

1. A humanized immunoglobulin having binding specificity for B7-2, said immunoglobulin comprising an antigen binding region of nonhuman origin and at least a portion of an immunoglobulin of human origin.

2. The humanized immunoglobulin of Claim 1, wherein the portion of an immunoglobulin of human origin is derived from a human constant region.

3. The humanized immunoglobulin of Claim 2, wherein the human constant region comprises an IgG constant region.

4. The humanized immunoglobulin of Claim 3, wherein the human constant region contains a mutation capable of reducing the effector function of the immunoglobulin.

5. The humanized immunoglobulin of Claim 4, wherein the human constant region comprises an IgG2 constant region and a Valine amino acid at position 234 is substituted with Alanine and/or a Glycine amino acid at position 237 is substituted with Alanine.

6. The humanized immunoglobulin of claim 3, wherein the IgG constant region is selected from the group consisting of an IgG4 constant region and an IgG2 constant region.

7. The humanized immunoglobulin of Claim 1, wherein the antigen binding region is of rodent origin.

8. The humanized immunoglobulin of Claim 1, wherein the antigen binding region comprises a complementarity determining region of rodent origin, and the portion of an immunoglobulin of human origin is derived from a human framework region.

9. The humanized immunoglobulin of Claim 8, wherein the complementarity determining region is derived from 3D1 monoclonal antibody.

10. A humanized immunoglobulin having binding specificity for B7-2, comprising a constant region of human origin and an antigen binding region, wherein said antigen binding region comprises:

a) a complementarity determining region derived from an antibody of rodent origin that binds to B7-2, and

b) a framework region derived from human origin.

11. The humanized immunoglobulin of Claim 10, wherein said immunoglobulin can compete with murine 3D1 for binding to B7-2.

12. The humanized immunoglobulin of Claim 11, wherein the antigen binding region comprises a light chain and a heavy chain, said light and heavy chains each having three complementarity determining regions derived from the 3D1 antibody.

13. The humanized immunoglobulin of Claim 12, wherein the framework region of the antigen binding region of the light chain is derived from the light chain of the H2F antibody.

14. The humanized immunoglobulin of Claim 13, wherein the framework region of the antigen binding region of the heavy chain is derived from the heavy chain of the human I2R antibody.

15. A humanized immunoglobulin having binding specificity for B7-2 derived from the cell line deposited with the ATCC, Accession No. CRL-12524.

16. A humanized immunoglobulin having a binding specificity for B7-2 comprising a heavy chain and a light chain,

the light chain comprising a complementarity determining region derived from an antibody of nonhuman origin which binds B7-2 and a framework region derived from a light chain of human origin, and

the heavy chain comprising a complementarity determining region derived from an antibody of nonhuman origin which binds B7-2 and a framework region derived from a heavy chain of human origin.

17. The humanized immunoglobulin of claim 16, wherein the immunoglobulin can compete with murine 3D1 for binding to B7-2.

18. The humanized immunoglobulin of Claim 16, wherein the light chain comprises three complementarity determining regions derived from the light chain of the 3D1 antibody, and the heavy chain comprises three complementarity determining regions derived from the heavy chain of the 3D1 antibody.

19. The humanized immunoglobulin of Claim 16, wherein the light chain of human origin is the light chain of the H2F antibody.

20. The humanized immunoglobulin of claim 16, wherein the heavy chain of human origin is the human I2R antibody.

21. A humanized immunoglobulin light chain having binding specificity for B7-2 comprising CDR1, CDR2 and CDR3 of the light chain of murine 3D1 antibody, and a human light chain framework region.

22. The humanized immunoglobulin light chain of Claim 21, wherein the human framework region is derived from the light chain of the H2F antibody.

23. The humanized immunoglobulin light chain of Claim 22, wherein the light chain comprises a variable region of SEQ ID NO: 8.

24. An isolated nucleic acid comprising a nucleic acid selected from the group consisting of:

a) SEQ ID NO:7,

b) a nucleic acid encoding the amino acid sequence of SEQ ID NO:8,

c) a nucleic acid which hybridizes to the nucleic acid according to a) or b) under stringent hybridization conditions, and

d) a nucleic acid which is the complement of the nucleic acid according to a) or b).

25. A humanized immunoglobulin heavy chain specific for B7-2 comprising CDR1, CDR2 and CDR3 of the heavy chain of the 3D1 antibody, and a human heavy chain framework region.

26. The humanized immunoglobulin heavy chain of Claim 25, wherein the human framework region is derived from the heavy chain of the human I2R antibody.

27. The humanized immunoglobulin heavy chain of Claim 26, wherein the heavy chain comprises a variable region of SEQ ID NO:6.

28. An isolated nucleic acid comprising a nucleic acid selected from the group consisting of:

b) SEQ ID NO: 5,

b) a nucleic acid encoding the amino acid sequence of SEQ ID NO:6,

c) a nucleic acid which hybridizes to the nucleic acid according to a) or b) under stringent hybridization conditions, and

d) a nucleic acid which is the complement of the nucleic acid according to a) or b).

29. A humanized immunoglobulin which specifically binds to B7-2 comprising:

a) a humanized light chain comprising three light chain complementarity determining regions from the mouse 3D1 antibody and a light chain variable region framework sequence from a human immunoglobulin light chain, and

b) a humanized heavy chain comprising three light chain complementarity determining regions from the mouse 3D1 antibody and a heavy chain variable region framework sequence from a human immunoglobulin heavy chain.

30. An expression vector comprising a fused gene encoding a humanized immunoglobulin light chain, said gene comprising a nucleotide sequence encoding a CDR derived from a light chain of a nonhuman antibody having binding specificity for B7-2 and a framework region derived from a light chain of human origin.

31. The expression vector of Claim 30, wherein the nonhuman antibody is murine 3D1 antibody.

32. A host cell comprising the expression vector of Claim 30.

33. An expression vector comprising a fused gene encoding a humanized immunoglobulin heavy chain, said gene comprising a nucleotide sequence encoding a CDR derived from a heavy chain of a nonhuman antibody having binding specificity for B7-2 and a framework region derived from a heavy chain of human origin.

34. The expression vector of Claim 33, wherein the nonhuman antibody is murine 3D1 antibody.

35. A host cell comprising the expression vector of Claim 33.

36. A host cell comprising nucleic acid encoding the humanized immunoglobulin of Claim 1.

37. A host cell comprising a first recombinant nucleic acid encoding a humanized immunoglobulin light chain and a second recombinant nucleic acid encoding a humanized immunoglobulin heavy chain, said first nucleic acid comprising a nucleotide sequence encoding a CDR derived from the light chain of murine 3D1 antibody and a framework region derived from a light chain of human origin; and said second nucleic acid comprising a nucleotide sequence encoding a CDR derived from the heavy chain of murine 3D1 antibody and a framework region derived from a heavy chain of human origin.

38. A method of preparing a humanized immunoglobulin comprising maintaining a host cell of Claim 37 under conditions appropriate for expression of a humanized

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immunoglobulin, wherein humanized immunoglobulin chains are expressed and a humanized immunoglobulin is produced.

39. The method of Claim 38, further comprising the step of isolating the humanized immunoglobulin.

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40. A fused gene encoding a humanized immunoglobulin light or heavy chain comprising:

a) a first nucleic acid sequence encoding an antigen binding region derived from murine 3D1 monoclonal antibody; and

b) a second nucleic acid sequence encoding at least a portion of a constant region of an immunoglobulin of human origin.

41. A method of inhibiting the interaction of a first cell bearing a B7-2 receptor with a second cell bearing B7-2, comprising contacting said first cell with an effective amount of a humanized immunoglobulin of Claim 1.

42. A method of modulating an immune response of a patient having a transplanted organ, tissue, cell or the like comprising administering an effective amount of the humanized immunoglobulin of Claim 1 in a carrier.

43. A method for treating a patient having a transplanted organ, tissue or cell, comprising administering a therapeutically effective amount of the humanized antibody of Claim 1.

44. The method of claim 43, wherein the carrier is pharmaceutical carrier.

45. A method of treating an autoimmune disease associated with modulation of the B7-2 molecule, comprising administering to a patient an effective amount of a humanized immunoglobulin of Claim 1 in a carrier, wherein treatment of the autoimmune disease occurs.

46. A pharmaceutical composition comprising the antibody of claim 1, and a pharmaceutically acceptable carrier.

47. A method of treating a patient with a disease selected from the group consisting of: autoimmune diseases, infectious diseases, inflammatory disorders, systemic lupus erythematosus, diabetes mellitus, insulitis, arthritis, inflammatory bowel disease, inflammatory dermatitis, and multiple sclerosis, comprising administering a therapeutically effective amount of a humanized immunoglobulin specific to B7-2 to the patient.

48. A method of treating a disease that is modulated by B7-2 comprising administering a therapeutically effective amount of the humanized antibody of Claim 1.

49. A method of making a humanized immunoglobulin having binding specificity for B7-2, said immunoglobulin comprising an antigen binding region of nonhuman origin and at least a portion of an immunoglobulin of human origin, comprising the steps of:

(a) determining the complementarity determining regions of an antibody of nonhuman origin which has binding specificity for B7-2;

(b) obtaining a human antibody having a framework region amino acid sequence suitable for grafting of the complementarity determining regions determined in (a), and

(c) grafting the complementarity determining regions of (a) into the framework region of the human antibody of (b),

wherein a humanized immunoglobulin having binding specificity for B7-2 is made.

50. The method of claim 49, wherein the antibody of nonhuman origin is of murine origin.

51. A method for determining the presence or absence of B7-2 in a sample comprising the steps of:

a) contacting said sample with a humanized antibody specific to B7-2 sufficiently to allow formation of a complex between B7-2 and the anti-B7-2 antibody, and

b) detecting the presence or absence of said complex formation.

52. A method for treating a patient with a disease selected from the group consisting of: autoimmune diseases, infectious diseases, inflammatory disorders, systemic lupus erythematosus, diabetes mellitus, insulitis, asthma, arthritis, inflammatory bowel disease, inflammatory dermatitis, and multiple sclerosis, comprising administering a therapeutically effective amounts of a humanized immunoglobulin specific to B7-1 and a therapeutically effective amount of a humanized immunoglobulin specific to B7-2.

53. A method of modulating an immune response of a patient having a transplanted organ, tissue, cell or the like comprising administering an effective amount of the humanized immunoglobulin specific to B7-1 and an effective amount of a humanized immunoglobulin specific to B7-2 in a carrier.

54. A method for transplanting cells to a patient in need thereof, comprising:

a) obtaining cells from a donor,

b) contacting the cells with an immunoglobulin specific to B7-1, an immunoglobulin specific to B7-2 and recipient cells from the patient for a period of time sufficient for tolerance induction, thereby obtaining a mixture, and

c) introducing the mixture to the patient.

55. The method of Claim 54, wherein the cells from the donor are derived from bone marrow or blood.

56. The method of Claim 55, wherein the recipient cell is a lymphocyte.

57. The method of Claim 56, wherein the period of time is between about 12 hours and about 48 hours.

58. The method of Claim 57, wherein the period of time is about 36 hours.

59. The method of Claim 54, wherein the patient has a disease that is selected from the group consisting of: a proliferative disease, anemia and myeloid dysplasia syndrome.

60. The method of Claim 59, wherein the proliferative disease is selected from the group consisting of: leukemia, lymphoma and cancer.

61. The method of Claim 59, wherein the anemia is selected from the group consisting of: sickle-cell anemia, thalassemia and aplastic anemia.

62. A method for transplanting cells to a patient in need thereof, comprising:

a) obtaining cells from a donor,

b) contacting the cells with an immunoglobulin specific to B7-1, an immunoglobulin specific to B7-2, and tissue, organ or cells that express MHC Class I antigen, B7-1 and B7-2 molecules, for a period of time sufficient for tolerance induction, thereby obtaining a mixture, and

c) introducing the mixture to the patient.

63. The method of Claim 62, wherein the cells derived from the donor are derived from bone marrow, stem cells or immature blood cells.